

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Diseases

Section Editor: Stephen B. Hanauer, MD

The Role of Capsule Endoscopy in IBD

Jonathan A. Leighton, MD
Associate Professor
Director, IBD Clinic
Mayo Clinic, Arizona

G&H What challenges in diagnosing inflammatory bowel disease led to the use of capsule endoscopy?

JL When diagnosing inflammatory bowel disease (IBD), in particular Crohn's disease (CD), identifying involvement of the small bowel can present a challenge. In patients with CD, 20–30% present with small bowel lesions. Diagnosis can be difficult when the disease is more proximal or ileal intubation during colonoscopy is not possible. Historically, the small bowel has been very difficult to evaluate endoscopically. With push enteroscopy, only the first 25–30% of the small bowel can be accessed. A colonoscopy can access only the distal few centimeters of the ileum. The majority of the small bowel, which is several feet long, has been very difficult to visualize endoscopically. Thus, diseases in this area have been difficult to diagnose, often leading physicians to resort to intraoperative enteroscopy, where the intestine is examined surgically. With CD, the difficulty in evaluating disease activity involving the small bowel has spurred interest in the use of capsule endoscopy.

Another clinical challenge that has led to the use of capsule endoscopy is obscure gastrointestinal bleeding. Approximately 5% of all gastrointestinal bleeding is thought to be due to lesions located in the small bowel. The difficulty in visualizing the small intestine has made identifying the bleeding source problematic and thus capsule endoscopy has been helpful. In approximately 10–15% of patients with obscure gastrointestinal bleeding, capsule endoscopy identifies mucosal breaks involving the small bowel, some of which are due to CD.

G&H What have studies evaluating capsule endoscopy in CD found?

JL Several studies have evaluated the use of capsule endoscopy in diagnosing patients with both suspected and established CD of the small bowel, comparing capsule endoscopy with the traditional colonoscopy with ileoscopy, barium small bowel follow-through (SBFT), and other radiologic modalities. Although many of these studies have been small retrospective analyses, they have shown an advantage for capsule endoscopy in terms of both the yield and sensitivity for detecting small bowel lesions.

One of the challenges with these studies is that many of the patients enrolled were already known to have a negative SBFT. Therefore, if the capsule reveals disease in the small bowel, the findings may be biased toward showing a greater benefit for capsule endoscopy than for SBFT.

Our group conducted a meta-analysis, currently in press, of all of the prospective comparative studies evaluating capsule endoscopy in CD. Combining these studies can be confusing, since terminology, types of lesions, and patient characteristics vary. Many studies of capsule endoscopy combined patients with established CD and suspected CD, which can confound the results. Therefore, in our analysis, we separated these two groups of patients in order to determine the value of capsule endoscopy in established CD and suspected CD. Overall, we found that capsule endoscopy did have a distinct advantage over other modalities, including SBFT, computed tomography (CT) enterography, and magnetic resonance (MR) enterography. This advantage was more predominant among patients with established CD; the same advantage was not seen in patients with suspected CD. These findings may be due to a type 2 error, as the total number of patients evaluated was relatively small. However, there did appear to be a clear advantage for capsule endoscopy for patients with known disease who are still experiencing symptoms but for whom other diagnostic tests did not detect disease presence. In other words, for patients with known CD, capsule endoscopy appears to have an advantage in diagnosing small bowel involvement that was not previously identified. Capsule endoscopy is likely also useful in patients with suspected CD, but further studies are needed to confirm this application.

G&H Based on findings thus far, what might be the appropriate role for capsule endoscopy in IBD at the present time?

JL When a patient presents with suspected or known CD, a colonoscopy and/or ileoscopy should be performed. If upper tract symptoms are present, an upper endoscopy should be performed. In addition, if small bowel disease is suspected, some type of small bowel imaging should be performed. If CD is not detected but is still suspected, then a capsule endoscopy would be a logical next step. It may be that capsule endoscopy should be the first step, if no obstruction or stricture is suspected.

More studies are needed in order to determine the role and timing of capsule endoscopy for patients suspected of having CD. How soon should a capsule endoscopy be used in such patients? It may be that this modality should be employed immediately following a colonoscopy and ileoscopy, rather than waiting until after radiography. Further studies will help clarify the role of capsule endoscopy in this setting.

G&H Are such studies ongoing?

JL Studies are continuing, and right now a prospective controlled trial to evaluate capsule endoscopy for suspected CD is being developed.

G&H Are there cautions to be aware of with capsule endoscopy use?

JL Capsule retention is the major risk with capsule endoscopy. If there is a stricture in the intestine the capsule could be retained, in which case surgery might be necessary in order to remove it. Among normal control patients, the incidence rate of a capsule being retained is close to 0%. For patients with obscure bleeding, the rate is somewhat higher, approximately 1–2%, sometimes due to CD or nonsteroidal anti-inflammatory drug (NSAID) enteropathy. Among all patients with CD, the rate is likely even higher, perhaps up to 7%, since the likelihood of a stricture being present is higher.

Many patients in whom the capsule becomes stuck may not have CD, but rather a different condition. When studies of capsule endoscopy in patients with obscure gastrointestinal bleeding first began, it was found that capsule retention occurred most commonly among patients with NSAID enteropathy, also known as diaphragm disease. NSAIDs can irritate the small intestine, and this irritation can have a similar appearance to that of CD, although the pathology is different. Neither x-rays nor CT appear to detect this condition well, but the capsule can become stuck between the thin diaphragms present, which alerts the physician to the presence of CD or diaphragm disease.

Other conditions that could lead to capsule retention include radiation enteritis or anastomotic strictures from previous surgery.

G&H Is it possible to determine whether the patient has CD or diaphragm disease?

JL No, because many patients with strictures do not have symptoms.

G&H How should capsule endoscopy be used in this situation?

JL If a patient presents with suspected or known CD and obstructive symptoms, the current recommendation is not to employ capsule endoscopy immediately. Instead, some type of radiologic imaging should be conducted—SBFT, CT enterography, or MR enterography. Depending upon the results, capsule endoscopy may be utilized. If there is evidence of a tight stricture that risks capsule retention, capsule endoscopy would not be recommended.

However, there is another consideration for patients with CD and recurrent abdominal pain. Some of these patients may have an occult stricture that is being overlooked by other modalities. There is evidence that for patients with negative x-rays and in whom the capsule becomes stuck, surgery is generally beneficial. Many of these patients' symptoms improve. Some physicians consider a retained capsule to be helpful because it indicates a previously undiagnosed lesion, and can lead to surgery that is able to resolve the symptoms. In our clinic, if a patient presents with pain or obstructive symptoms but no cause is identified, we may occasionally use capsule endoscopy knowing in advance that the capsule may become stuck, since this may help in diagnosing the problem.

There is a patency capsule, developed by Given Imaging, made of a lactose body and wax plugs on the end that dissolves in the body but has a radio frequency identification tag that can be followed. This capsule has been approved in Europe, although not yet in the United States, where studies are still ongoing. This capsule can be given to patients with known strictures. If the capsule is excreted intact, then it is considered safe to proceed with capsule endoscopy. If the patency capsule dissolves before excretion, then it is likely that a capsule endoscope will become stuck, and is therefore not recommended.

G&H What are other challenges in using capsule endoscopy to diagnose CD?

JL One of the issues in diagnosing CD with any modality, including capsule endoscopy, is the specificity of the finding. When a mucosal break is detected in the small bowel, how can one be certain that the lesion is due to

CD? Drugs, especially NSAIDs, and infection may also cause similar lesions and therefore it is not always certain that the lesion is due to CD. In addition, in healthy people, studies have suggested that the rate of occurrence of lesions of uncertain significance may be as high as 13%.

Efforts to improve biopsy capabilities and remote control capabilities with the capsule are ongoing. It may be possible to develop capsules that will enable physicians to examine the lesion in greater depth, or to take tissue biopsies. However, such capabilities will not be available in the near future.

It may be possible to complement capsule endoscopy with enteroscopy, such as the double-balloon technique, enabling a larger part of the bowel to be seen. In addition, double-balloon enteroscopy allows for the biopsy of lesions. Because there is not one single confirmatory

test to determine whether a lesion is due to CD or not, it is necessary to combine several parameters. Radiologic, pathologic, and serologic tests should all be considered, and patients should be questioned about NSAID use and other potential causes.

Suggested Reading

Davis BR, Harris H, Vitale GC. The evolution of endoscopy: wireless capsule cameras for the diagnosis of occult gastrointestinal bleeding and inflammatory bowel disease. *Surg Innov.* 2005;12:129-133.

Legani P, Kornbluth A. Video capsule endoscopy in inflammatory bowel disease 2005. *Curr Opin Gastroenterol.* 2005;21:438-442.

Kornbluth A, Legani P, Lewis BS. Video capsule endoscopy in inflammatory bowel disease: past, present, and future. *Inflamm Bowel Dis.* 2004;10:278-285.

Triester SL, Leighton JA, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. *Am J Gastroenterol.* 2006. In press.